

April 26, 2006

Lynne Jones  
Metal Carboxylates Coalition  
SOCMA  
1850 M Street NW, Suite 700  
Washington, DC 20036

Dear Ms. Jones,

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the revised Potassium 2-ethylhexanoate and Calcium bis(2-ethylhexanoate) Category posted on the ChemRTK HPV Challenge Program Web site on August 27, 2004. I commend the Metal Carboxylates Coalition for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Coalition advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: [oppt.ncic@epa.gov](mailto:oppt.ncic@epa.gov) and [chem.rtk@epa.gov](mailto:chem.rtk@epa.gov).

If you have any questions about this response, please contact Mark Townsend, Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at [tsca-hotline@epa.gov](mailto:tsca-hotline@epa.gov).

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director  
Risk Assessment Division

Enclosure

cc: W. Penberthy  
J. Willis

**EPA Comments on Chemical RTK HPV Challenge Submission:  
Potassium 2-ethylhexanoate and Calcium bis(2-ethylhexanoate) Category**

**Summary of EPA Comments**

The sponsor, the Metal Carboxylates Coalition, submitted a test plan and robust summaries to EPA for the revised Potassium 2-ethylhexanoate and Calcium bis(2-ethylhexanoate) category, dated June 23, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on August 27, 2004. The category consists of Potassium 2-ethylhexanoate (CAS No. 3164-85-0) and Calcium bis(2-ethylhexanoate)(CAS No. 136-51-6).

EPA has reviewed this submission and has reached the following conclusions:

1. General. The submitter needs to provide data or a technical discussion to support the assertion that the toxicity of the salts is equivalent to that of the separate metal ions and their respective organic acids.
2. Category Definition. The category is clearly defined.
3. Category Justification. The submitter's support for grouping these chemicals is reasonable.
4. Physicochemical Properties. The submitter needs to provide measured melting point data and reliable water solubility data for the calcium salt, and address deficiencies in the robust summaries.
5. Environmental Fate. EPA agrees with the submitter that no further testing is needed. However, the submitter needs to provide a technical discussion for the photodegradation endpoint. Also, a technical discussion needs to be provided for the stability in water endpoint, referencing the dissociation of the metal salt complexes. The submitter needs to address deficiencies in the robust summaries.
6. Health Effects. Adequate data were submitted for all SIDS endpoints for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.
7. Ecological Effects. EPA reserves judgement for these endpoints until deficiencies in the robust summaries for 2-ethylhexanoic acid are addressed.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

**EPA Comments on the Potassium 2-ethylhexanoate and Calcium  
Bis(2-ethylhexanoate) Category Challenge Submission**

**General**

This submission included robust summaries for calcium bis(2-ethylhexanoate) and the SIDS Dossier for 2-ethylhexanoic acid. Summaries for potassium 2-ethylhexanoate submitted with the original Metal Carboxylates submission were used for this review.

**Category Definition**

The category consists of two substances, potassium 2-ethylhexanoate and calcium bis(2-ethylhexanoate). The definition is clear and unambiguous.

## **Category Justification**

The combining of the two substances is adequately supported in that toxic effects are likely due primarily to 2-ethylhexanoate. The counter ions, an alkali metal and alkaline earth metal, respectively, are abundant in biological systems, well characterized, and are not expected to contribute directly to toxicity.

## **Test Plan**

On 22 May 2003, EPA commented that the original test plan did not adequately support the statement by the submitter that the bioavailability (and therefore the environmental fate, aquatic toxicity, and mammalian toxicity) of metal carboxylate salts would be equivalent to that of the separate metal ions and organic acids. The original test plan did not address the issue of the stability of metal-ligand complexes and only provided data for the acid/base (pKa, pKb) dissociation constants. The revised test plan still has not adequately addressed the use of the data on the dissociation products for the sponsored metal-ligand complexes. The submitter needs to provide a technical discussion on dissociation, with appropriate supporting experimental data on the dissociation of the metal-ligand complexes, and the bioequivalency of the dissociation products to the sponsored substances. As examples of more detailed discussions EPA refers the submitter to the technical discussions provided in the more recent submissions (especially the cobalt complexes) from the Metal Carboxylates Coalition (<http://www.epa.gov/chemrtk/metalcarb/c14172tc.htm>).

### **Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)**

Adequate data were submitted for the melting point (potassium 2-ethylhexanoate), boiling point, vapor pressure and partition coefficient endpoints for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

*Melting point.* The submitter needs to provide measured melting point data for calcium 2-ethylhexanoate, according to OECD TG 102. EPA refers the submitter to Nora et. al (2002) at ([www.mrw.interscience.wiley.com/ueic](http://www.mrw.interscience.wiley.com/ueic)).

*Water solubility.* Adequate data were submitted for potassium 2-ethylhexanoate. For the calcium salt, the submitted data range from 5 mg/L (estimated) to as high as 50 g/L (aquatic toxicity data). The submitter needs to provide measured water solubility data for the calcium salt according to OECD TG 105.

### **Environmental Fate (photodegradation, stability in water, biodegradation and fugacity)**

Adequate data were submitted for the photodegradation, biodegradation and fugacity endpoints for the purposes of the HPV Challenge Program.

*Stability in water.* A technical discussion needs to be included describing the multiple equilibria that occur during the dissociation of metal carboxylates. Although pH will have a strong effect on the stability of the metal-ligand complex, the tendency of the complex to dissociate is described by the metal-ligand dissociation constant ( $K_f$ ) and not the acid-base dissociation constant (pKa and pKb). The submitter needs to distinguish these two dissociation equilibria in the discussion, especially as they pertain to water solubility.

## Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

All SIDS mammalian toxicity endpoints are satisfied by data on 2-ethylhexanoic acid. Although data for calcium octanoate (CAS No. 6107-56-8) were submitted for the acute toxicity and genetic toxicity (gene mutations) endpoints, there was no discussion in the test plan about the relevance of the analog.

## Ecological Effects (fish, invertebrates, and algae)

EPA reserves judgement for these endpoints. Critical data elements missing from key robust summaries for 2-ethylhexanoic acid need to be submitted before an independent evaluation can be rendered.

## **Specific Comments on the Robust Summaries**

### General

The following comments apply particularly to the physicochemical and environmental fate robust summaries. In general, they did not provide enough detail. The submitter should consult EPA guidance documents for the preparation of robust summaries (<http://www.epa.gov/opptintr/chemrtk/guidocs.htm>).

### Physicochemical Properties

The submitter needs to prepare robust summaries for the data cited in the test plan for all physicochemical endpoints.

*Vapor pressure.* Estimation methods are generally not reliable for inorganic salts, as the methods were derived for neutral organics. However, they are adequate in this case for the purposes of the HPV Challenge Program because they are near or below the guideline threshold value of  $1 \times 10^{-5}$  Pa. The submitter needs to state the limitations of the estimation method.

### Environmental Fate

*Photodegradation.* The submitter needs to provide a technical discussion on the potential for direct photolysis for the category members.

*Fugacity.* The submitter needs to prepare robust summaries for the estimated data cited in the test plan, including the modeling parameters used, since fugacity modeling has not been validated for salts.

### Health Effects

*Genetic toxicity (gene mutations).* The summary needs to identify the positive controls for the calcium salt.

### Ecological Effects

The submitter needs to provide pH, dissolved oxygen, water temperature, number of replicates per test, and water hardness where applicable in the key robust summaries.

## **Followup Activity**

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.